

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: John C. Salerno

Application No.: 09/398,405

Group Art Unit: 1642

Filed: September 16, 1999

Examiner: S. Ungar

For: ACTIVATORS OF ENDOTHELIAL NITRIC OXIDE SYNTHASE

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231

on 9/28/01 Christina McSweeney
Date Signature

Christina McSweeney
Typed or printed name of person signing certificate

REPLY TO SECOND RESTRICTION REQUIREMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Responsive to the Restriction Requirement dated June 5, 2001, the claim of Group 35 (Claims 31, 32 and 49), drawn to methods of activating endothelial nitric oxide synthase (ENOS) wherein the activator is a peptide, and treating a disease comprising administering a peptide, is elected for prosecution with traverse. Applicant reserves the right to file a divisional or continuing application, or take such other appropriate action as deemed necessary to protect the invention(s) of Groups 1-34 and 36-57. Applicants do not hereby abandon or waive any rights in the invention(s) of these other groups. Reconsideration and modification of the restriction requirement is requested.

An extension of time to respond to the Restriction Requirement is respectfully requested. A Petition for an Extension of Time and the appropriate fee are being filed concurrently.

The inventions claimed in the subject application arise from the discovery of the existence and identity of regulatory peptides of constitutive nitric oxide synthases ("NOS"), including endothelial and neuronal NOS, that are not found in inducible NOS. This discovery, *inter alia*, gave rise to the ability to selectively inhibit or activate a constitutive NOS (ENOS, NNOS) or inducible NOS (INOS).

Group 35 (Claims 31, 32 and 49) is drawn to methods of activating endothelial nitric oxide synthase wherein the activator is a peptide, and methods of treating a disease by administering a peptide.

The method of Claim 32 comprises contacting the endothelial nitric oxide synthase with an effective amount of an agent of Claim 19. Claim 19 defines activators of constitutive NOS, embodied as the regulatory peptides of the NOS enzymes: it is drawn to a constitutive nitric oxide synthase activator peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:4-9 and activating fragments and derivatives of SEQ ID NO: 4-9. Claim 49 is drawn to a method of treating a disease modulated by production of nitric oxide by endothelial nitric oxide synthase in a mammal. The method of Claim 49 comprises contacting the endothelial nitric oxide synthase with an effective amount of an agent of Claim 19.

Applicant's Attorney notes that in paragraph 8 on page 10 of the Office Action, the Examiner states that "Group 26 is further subject to election of a single disclosed species." The Office Action further states:

Claims 21 and 32 are generic to a plurality of disclosed patentably distinct species comprising peptides with different structures and functions, wherein the peptides are (a) SEQ ID NO: 4, (b) SEQ ID NO: 5, (c) SEQ ID NO: 6, (d) SEQ ID NO: 7, (e) SEQ ID NO: 8, (f) SEQ ID NO: 9.

Because this paragraph relates to the sequences set forth in Claim 19, Applicant's Attorney assumes for the purposes of this response that the Examiner intended to state that Group 35 (the elected group) is subject to election of a single disclosed species. Applicant's Attorney respectfully requests clarification of this paragraph.

Assuming that election of a single disclosed species is required, Applicant's Attorney elects the peptide of SEQ ID NO: 6. Applicant's Attorney respectfully traverses the Examiner's requirement of election of a single species. As stated above, the Examiner indicated that the claims are generic to species comprising "peptides with different structures and functions". However, as indicated in the Specification at page 15, lines 16-19, each of the sequences set forth in SEQ ID NO: 4-9 have a commonality of structure: they are all negatively charged loops of a NOS isoform. Furthermore, of the close structural and functional relationship among the three NOS isoforms (see, e.g., the Specification at page 25, line 17 *et seq.*), one of ordinary skill in the

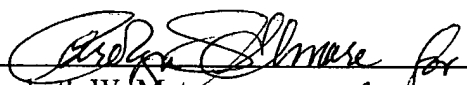
art would understand that the negatively charged loops would have a similar function in each isoform. Therefore, Applicant's Attorney requests that SEQ ID NO: 4-9 be examined concurrently.

Applicant additionally traverses the Examiner's requirement based on the clear statement in MPEP §803.04, and in the Official Gazette Notice dated November 19, 1996, regarding the examination of patent applications containing nucleotide sequences, which state that "...the Commissioner has decided sua sponte to partially waive the requirements of 37 C.F.R. 1.141 et seq. and permit a reasonable number of such nucleotide sequences to be claimed in a single application. Accordingly, in most cases, up to ten (10) independent and distinct nucleotide sequences will be examined in a single application without restriction." In accordance with these established guidelines, Applicant submits that the MPEP clearly contemplates inclusion of plural sequences in a single group. It is reasonable to examine up to ten nucleotide sequences in the subject application, and that therefore, the six sequences of SEQ ID NO: 4-9 can be recombined. Furthermore, these sequences are all short in length, and it would be possible to conduct a search with all six sequences as a single query. Nothing in the record suggests that the search related to these sequences would be out of the ordinary. Therefore Applicant requests that the Examiner reconsider the restriction and recombine the requested species for these reasons as well.

If the Examiner believes that a telephone conversation would expedite prosecution of the application, the Examiner is invited to call Elizabeth W. Mata at (915) 845-3558. If Elizabeth W. Mata cannot be reached, the Examiner is invited to call David E. Brook at (781) 861-6240.

Respectfully submitted,

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